AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1-36 (cancelled).

37. (currently amended) A method of using a computer for selecting at least one of a plurality of chemical entities based on its ability to associate with all or part of a molecule or molecular complex comprising a calcineurin A (CnA) binding pocket defined by structure coordinates of CnA amino acids 90, 91, 92, 118, 120, 121, 122, 150, 151, 156, 160, 199, 232, 253, 254, 256, 281, 282, 283, 284, 306, 311, 312, and 317 according to Figure 1;

wherein said computer comprises a machine-readable data storage medium comprising a data storage material encoded with said structure coordinates and wherein said method comprises the steps of:

a) producing a crystal of a molecular complex comprising amino acids 17-392 of CnA and amino acids 1-169 of CnB; intact FKBP12; and FK506;

b) determining the three-dimensional structure coordinates of the molecular complex by X-ray diffraction of the crystal;

c) identifying the structural coordinates of a CnA binding pocket of said molecular complex of CnA amino acids 90, 91, 92, 118, 120, 121, 122, 150, 151, 156, 160, 199, 232, 253, 254, 256, 281, 282, 283, 284, 306, 311, 312, and 317, which coordinates fall within the range of those recited in Figure 1 ± a root mean square deviation from the backbone atoms of said amino acids of 1.5Å and encoding those coordinates on a data storage material;

d) utilizing ~~all or part of~~ said structure coordinates defining said CnA binding pocket and the structure coordinates of one of said plurality of chemical entities to position a chemical entity within all or part of the CnA binding pocket;

e) docking said chemical entity with all or part of the CnA binding pocket by employing computational means which utilize ~~all or part of~~ said structure coordinates defining said CnA binding pocket ~~or~~ and the chemical entity, wherein said docking utilizes energy minimization;

f) analyzing the results of said docking to quantify the association between said chemical entity and all or part of the CnA binding pocket;

g) optionally repeating steps d) through f) with another of said plurality of chemical entities; and

h) selecting at least one of said plurality of chemical entities that associates with all or part of the CnA binding pocket based on said quantified association of said chemical entity.

38. (currently amended) A method of using a computer for selecting at least one of a plurality of chemical entities based on its ability to associate with all or part of a molecule or molecular complex comprising a calcineurin A (CnA) binding pocket defined by structure coordinates of CnA amino acids 90, 91, 92, 118, 120, 121, 122, 150, 151, 156, 160, 199, 281, 282, 283, 306, 311, 232, and 254 according to Figure 1; wherein said computer comprises a machine-readable data storage medium comprising a data storage material encoded with said structure coordinates and wherein said method comprises the steps of:

a) producing a crystal of a molecular complex comprising amino acids 17-392 of CnA and amino acids 1-169 of CnB; intact FKBP12; and FK506;

b) determining the three-dimensional structure coordinates of the molecule or molecular complex by X-ray diffraction of the crystal;

c) identifying a CnA binding pocket of said molecule or molecular complex defined by structure coordinates of CnA amino acids 90, 91, 92, 118, 120, 121,

122, 150, 151, 156, 160, 199, 281, 282, 283, 306, 311, 232, and 254, which coordinates fall within the range of those recited in Figure 1 ± a root mean square deviation from the backbone atoms of said amino acids of 1.5Å and encoding those coordinates on a data storage material;

d) utilizing ~~all or part of~~ said structure coordinates defining said CnA binding pocket and the structure coordinates of one of said plurality of chemical entities to position a chemical entity within all or part of the CnA binding pocket;

e) docking said chemical entity with all or part of the CnA binding pocket by employing computational means which utilize ~~all or part of~~ said structure coordinates defining said CnA binding pocket and the chemical entity, wherein said docking utilizes energy minimization;

f) analyzing the results of said docking to quantify the association between said chemical entity and all or part of the CnA binding pocket;

g) optionally repeating steps d) through f) with another of said plurality of chemical entities; and

h) selecting at least one of said plurality of chemical entities that associates with all or part of the CnA binding pocket based on said quantified association of said chemical entity.

39. (currently amended) A method of using a computer for selecting at least one of a plurality of chemical entities based on its ability to associate with all or part of a molecule or molecular complex comprising a CnA/CnB binding pocket defined by structure coordinates of CnA amino acids 122, 124, 159, 160, 310, 312, 313, 314, 339, 341, 343, 344, 345, 347, 351, 352, 353, 354, 355, 356, 359, 360, and 363; and calcineurin B (CnB) amino acids 49, 50, 114, 115, 118, 119, 121, 122, 123, 124, 157, 158, 159, 161, and 162 according to Figure 1; wherein said computer comprises a machine-readable data storage medium comprising a data storage material encoded with said structure coordinates and wherein said method comprises the steps of:

a) producing a crystal of a molecular complex comprising amino acids 17-392 of CnA and amino acids 1-169 of CnB; intact FKBP12; and FK506;

b) determining the three-dimensional structure coordinates of the molecule or molecular complex by X-ray diffraction of the crystal;

c) identifying a CnA/CnB binding pocket of said molecule or molecular complex defined by structure coordinates of CnA amino acids 122, 124, 159, 160, 310, 312, 313, 314, 339, 341, 343, 344, 345, 347, 351, 352, 353, 354, 355, 356, 359, 360, and 363; and

calcineurin B (CnB) amino acids 49, 50, 114, 115, 118, 119, 121, 122, 123, 124, 157, 158, 159, 161, and 162, which coordinates fall within the range of those recited in Figure 1 ± a root mean square deviation from the backbone atoms of said amino acids of 1.5Å and encoding those coordinates on a data storage material;

d) utilizing ~~all or part of~~ said structure coordinates defining said CnA/CnB binding pocket and the structure coordinates of one of said plurality of chemical entities to position a chemical entity within all or part of the CnA/CnB binding pocket;

e) docking said chemical entity with all or part of the CnA/CnB binding pocket by employing computational means which utilize ~~all or part of~~ said structure coordinates defining said CnA/CnB binding pocket and the chemical entity, wherein said docking utilizes energy minimization;

f) analyzing the results of said docking to quantify the association between said chemical entity and all or part of the CnA/CnB binding pocket;

g) optionally repeating steps d) through f) with another of said plurality of chemical entities; and

h) selecting at least one of said plurality of chemical entities that associates with all

or part of the CnA/CnB binding pocket based on said quantified association of said chemical entity.

40. (currently amended) A method of using a computer for selecting at least one of a plurality of chemical entities based on its ability to associate with all or part of a molecule or molecular complex comprising a CnA/CnB binding pocket defined by structure coordinates of CnA amino acids 90, 91, 92, 118, 120, 121, 122, 124, 150, 151, 156, 159, 160, 199, 232, 253, 254, 256, 281, 282, 283, 284, 306, 310, 311, 312, 313, 314, 317, 339, 341, 343, 344, 345, 347, 351, 352, 353, 354, 355, 356, 359, 360, and 363; and CnB amino acids 49, 50, 114, 115, 118, 119, 121, 122, 123, 124, 157, 158, 159, 161, and 162 according to Figure;

wherein said computer comprises a machine-readable data storage medium comprising a data storage material encoded with said structure coordinates and wherein said method comprises the steps of:

a) producing a crystal of a molecular complex comprising amino acids 17-392 of CnA and amino acids 1-169 of CnB; intact FKBP12; and FK506;

b) determining the three-dimensional structure coordinates of the molecule or molecular complex by X-ray diffraction of the crystal;

c) identifying a CnA/CnB binding pocket of said molecule or molecular complex defined by structure coordinates of CnA amino acids 90, 91, 92, 118, 120, 121, 122, 124, 150, 151, 156, 159, 160, 199, 232, 253, 254, 256, 281, 282, 283, 284, 306, 310, 311, 312, 313, 314, 317, 339, 341, 343, 344, 345, 347, 351, 352, 353, 354, 355, 356, 359, 360, and 363; and CnB amino acids 49, 50, 114, 115, 118, 119, 121, 122, 123, 124, 157, 158, 159, 161, and 162, which coordinates fall within the range of those recited in Figure 1 ± a root mean square deviation from the backbone atoms of said amino acids of 1.5 Å and encoding those coordinates on a data storage material;

d) utilizing ~~all or part of~~ said structure coordinates defining said CnA/CnB binding pocket and the structure coordinates of one of said plurality of chemical entities to position a chemical entity within all or part of the CnA/CnB binding pocket;

e) docking said chemical entity with all or part of the CnA/CnB binding pocket by employing computational means which utilize ~~all or part of~~ said structure coordinates defining said CnA/CnB binding pocket or structure coordinates of the chemical entity, wherein said docking utilizes energy minimization;

f) analyzing the results of said docking to quantify the association between said chemical entity and all or part of the CnA/CnB binding pocket;

g) optionally repeating steps d) through f) with another of said plurality of chemical entities; and

h) selecting at least one of said plurality of chemical entities that associates with all or part of the CnA/CnB binding pocket based on said quantified association of said chemical entity.

41. (previously presented) The method according to any one of claims 37-40, further comprising the steps of:

i) contacting the selected chemical entity with said molecule or molecular complex; and

j) monitoring the association of the molecule or molecular complex with the selected chemical entity.

42. (previously presented) The method according to any one of claims 37-40, wherein the docking utilizes shape complementarity or is followed by molecular dynamics.

43. (previously presented) The method according to any one of claims 37-40, wherein the docking

is performed through visual inspection on a computer screen using a computer program capable of generating a three-dimensional graphical representation of said structure coordinates and structure coordinates of said chemical entity.

44. (previously presented) The method according to any one of claims 37-40, further comprising the steps of:

i) repeating steps d) to h) with a second set of a plurality of chemical entities that associate with all or another part of the binding pocket;

j) optionally, visually inspecting the relationship of the selected first and second chemical entities to each other in relation to the binding pocket on a computer screen using the three-dimensional graphical representation of the binding pocket and said selected first and second chemical entity; and

k) assembling the first and second chemical entities into a compound or complex that associates with all or part of said binding pocket by model building.

45-56. (cancelled).